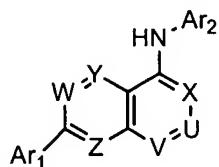


**Amendments to the Claims**

This listing of claims will replace all prior versions, and listings, of claims in the application.

1. (Currently amended) A compound of the formula:



or a pharmaceutically acceptable form salt or hydrate thereof, wherein:

V, X, W, Y and Z are each independently N or CR<sub>1</sub>, with the proviso that at least one of V and X is N;

U is N or CR<sub>2</sub>, with the proviso that if V and X are N, then U is CR<sub>2</sub>;

R<sub>1</sub> is independently selected at each occurrence from hydrogen, halogen, hydroxy, cyano, amino, -COOH, C<sub>1</sub>-C<sub>6</sub>alkyl, haloC<sub>1</sub>-C<sub>6</sub>alkyl, C<sub>1</sub>-C<sub>6</sub>alkoxy, C<sub>1</sub>-C<sub>6</sub>alkoxycarbonyl, haloC<sub>1</sub>-C<sub>6</sub>alkoxy and mono- and di-(C<sub>1</sub>-C<sub>6</sub>alkyl)amino;

R<sub>2</sub> is:

(i) hydrogen, halogen, cyano or nitro; or

(ii) a group of the formula -R<sub>c</sub>-M-A-R<sub>y</sub>, wherein:

R<sub>c</sub> is C<sub>0</sub>-C<sub>3</sub>alkyl, C<sub>2</sub>-C<sub>3</sub>alkenyl or C<sub>2</sub>-C<sub>3</sub>alkynyl, or is joined to R<sub>y</sub> or R<sub>z</sub> to form a 4- to 10-membered carbocycle or heterocycle that is substituted with from 0 to 2 substituents independently selected from R<sub>b</sub>;

M is a bond, O, S, SO, SO<sub>2</sub>, C(=O), OC(=O), C(=O)O, O-C(=O)O, C(=O)N(R<sub>z</sub>), N(R<sub>z</sub>)C(=O), N(R<sub>z</sub>)SO<sub>2</sub>, SO<sub>2</sub>N(R<sub>z</sub>), N(R<sub>z</sub>), OPO<sub>2</sub>(OR<sub>z</sub>) or PO<sub>2</sub>(OR<sub>z</sub>);

A is a bond or C<sub>1</sub>-C<sub>8</sub>alkyl substituted with from 0 to 3 substituents independently selected from R<sub>b</sub>; and

R<sub>y</sub> and R<sub>z</sub>, if present, are:

(a) independently:

(i) hydrogen or -COOH; or

(ii) C<sub>1</sub>-C<sub>8</sub>alkyl, C<sub>2</sub>-C<sub>8</sub>alkenyl, C<sub>2</sub>-C<sub>8</sub>alkynyl, C<sub>3</sub>-C<sub>8</sub>alkanone C<sub>2</sub>-C<sub>8</sub>alkanone, C<sub>2</sub>-C<sub>8</sub>alkyl ether, a 4- to 10-membered carbocycle or heterocycle, or

joined to R<sub>c</sub> to form a 4- to 10-membered carbocycle or heterocycle, each of which is substituted with from 0 to 6 substituents independently chosen from R<sub>b</sub>; or

(b) joined to form a 4- to 10-membered carbocycle or heterocycle that is substituted with from 0 to 6 substituents independently selected from R<sub>b</sub>;

Ar<sub>1</sub> and Ar<sub>2</sub> are independently selected from 5- to 10-membered carbocycles and

heterocycles, each of which is substituted with from 0 to 3 substituents

independently selected from groups of the formula LR<sub>a</sub>;

L is independently selected at each occurrence from a bond, O, S(O)<sub>m</sub>, C(=O), OC(=O), C(=O)O, O-C(=O)O, N(R<sub>x</sub>), C(=O)N(R<sub>x</sub>), N(R<sub>x</sub>)C(=O), N(R<sub>x</sub>)S(O)<sub>m</sub>, S(O)<sub>m</sub>N(R<sub>x</sub>) and N[S(O)<sub>m</sub>R<sub>x</sub>]S(O)<sub>m</sub>; wherein m is independently selected at each occurrence from 0, 1 and 2; and R<sub>x</sub> is independently selected at each occurrence from hydrogen and C<sub>1</sub>-C<sub>8</sub>alkyl;

R<sub>a</sub> is independently selected at each occurrence from:

(i) hydrogen, halogen, cyano and nitro; and

(ii) C<sub>1</sub>-C<sub>8</sub>alkyl, C<sub>2</sub>-C<sub>8</sub>alkenyl, C<sub>2</sub>-C<sub>8</sub>alkynyl, C<sub>2</sub>-C<sub>8</sub>alkyl ether, mono- and di-(C<sub>1</sub>-C<sub>8</sub>alkyl)amino and (3- to 10-membered heterocycle)C<sub>0</sub>-C<sub>6</sub>alkyl, each of which is substituted with from 0 to 6 substituents independently selected from R<sub>b</sub>; and

R<sub>b</sub> is independently chosen at each occurrence from:

(i) hydroxy, halogen, amino, aminocarbonyl, cyano, nitro, oxo and -COOH; and

(ii) C<sub>1</sub>-C<sub>8</sub>alkyl, C<sub>2</sub>-C<sub>8</sub>alkenylC<sub>4</sub>-C<sub>8</sub>alkenyl, C<sub>2</sub>-C<sub>8</sub>alkynylC<sub>4</sub>-C<sub>8</sub>alkynyl, C<sub>1</sub>-C<sub>8</sub>alkoxy, C<sub>1</sub>-C<sub>8</sub>alkanoyl, C<sub>2</sub>-C<sub>8</sub>alkoxycarbonyl, C<sub>2</sub>-C<sub>8</sub>alkanoyloxy, C<sub>1</sub>-C<sub>8</sub>alkylthio, C<sub>2</sub>-C<sub>8</sub>alkyl ether, phenylC<sub>0</sub>-C<sub>8</sub>alkyl, phenylC<sub>1</sub>-C<sub>8</sub>alkoxy, mono- and di-(C<sub>1</sub>-C<sub>6</sub>alkyl)amino, (SO<sub>2</sub>)C<sub>1</sub>-C<sub>8</sub>alkyl, (4- to 7-membered heterocycle)C<sub>0</sub>-C<sub>8</sub>alkyl, -PO<sub>3</sub>(R<sub>w</sub>)<sub>2</sub> and -OPO<sub>3</sub>(R<sub>w</sub>)<sub>2</sub>, wherein each R<sub>w</sub> is independently chosen from hydrogen, C<sub>1</sub>-C<sub>8</sub>alkyl, phenylC<sub>0</sub>-C<sub>8</sub>alkyl and (5- to 7-membered heterocycle)C<sub>0</sub>-C<sub>8</sub>alkyl;

wherein each of (ii) is substituted with from 0 to 3 substituents

independently chosen from hydroxy, halogen, amino, aminocarbonyl, cyano, nitro, oxo, -COOH, C<sub>1</sub>-C<sub>8</sub>alkyl, C<sub>1</sub>-C<sub>8</sub>alkoxy, C<sub>1</sub>-C<sub>8</sub>alkoxycarbonyl, C<sub>2</sub>-C<sub>8</sub>alkanoyloxy, C<sub>1</sub>-C<sub>8</sub>alkylthio, C<sub>2</sub>-C<sub>8</sub>alkyl etherC<sub>4</sub>-C<sub>8</sub>alkyl ether, hydroxyC<sub>1</sub>-C<sub>8</sub>alkyl, haloC<sub>1</sub>-C<sub>8</sub>alkyl, phenylC<sub>0</sub>-C<sub>8</sub>alkyl, mono- and di-(C<sub>1</sub>-C<sub>6</sub>alkyl)amino, (SO<sub>2</sub>)C<sub>1</sub>-C<sub>8</sub>alkyl and (5- to 7-membered heterocycle)C<sub>0</sub>-C<sub>8</sub>alkyl; and

wherein the compound or pharmaceutically acceptable form-salt or hydrate thereof comprises at least one carboxylic acid, phosphate or phosphonate group.

2. (Currently amended) A compound or pharmaceutically acceptable form-salt or hydrate thereof according to claim 1, wherein U is C-R<sub>2</sub>.

3. (Currently amended) A compound or pharmaceutically acceptable form-salt or hydrate thereof according to claim 2, wherein X and V are N.

4. – 7. (Cancelled)

8. (Currently amended) A compound or pharmaceutically acceptable form-salt or hydrate thereof according to claim 1, wherein W, Y and Z are each CH.

9. (Currently amended) A compound or pharmaceutically acceptable form-salt or hydrate thereof according to claim 2, wherein R<sub>2</sub> is a group of the formula – R<sub>c</sub>-M-A-R<sub>y</sub>, R<sub>c</sub> is C<sub>1</sub>-C<sub>3</sub>alkyl, and R<sub>2</sub> comprises a carboxylic acid, phosphate or phosphonate group.

10. (Currently amended) A compound or pharmaceutically acceptable form-salt or hydrate thereof according to claim 9, wherein R<sub>2</sub> comprises a carboxylic acid group.

11. (Currently amended) A compound or pharmaceutically acceptable form-salt or hydrate thereof according to claim 10, wherein the carboxylic acid group is a substituent of a heterocyclic ring.

12. (Currently amended) A compound or pharmaceutically acceptable form-salt or hydrate thereof according to claim 9, wherein R<sub>2</sub> comprises a phosphate or phosphonate group.

13. (Currently amended) A compound or pharmaceutically acceptable form-salt or hydrate thereof according to claim 1, wherein Ar<sub>1</sub> and Ar<sub>2</sub> are independently selected from phenyl and 6-membered aromatic heterocycles, each of which is substituted with 0, 1 or 2 substituents independently selected from groups of the formula LR<sub>a</sub>.

14. (Currently amended) A compound or pharmaceutically acceptable form salt or hydrate thereof according to claim 13, wherein:

Ar<sub>1</sub> is phenyl or pyridyl, each of which is substituted with from 0 to 2 substituents independently selected from halogen, hydroxy, cyano, amino, nitro, mono- and di-(C<sub>1</sub>-C<sub>6</sub>alkyl)amino, C<sub>1</sub>-C<sub>6</sub>alkyl, haloC<sub>1</sub>-C<sub>6</sub>alkyl, C<sub>1</sub>-C<sub>6</sub>alkoxy and haloC<sub>1</sub>-C<sub>6</sub>alkoxy; and

Ar<sub>2</sub> is phenyl or pyridyl, each of which is substituted with from 0 to 2 substituents independently selected from halogen, hydroxy, cyano, amino, nitro, mono- and di-(C<sub>1</sub>-C<sub>6</sub>alkyl)amino, C<sub>1</sub>-C<sub>6</sub>alkyl, haloC<sub>1</sub>-C<sub>6</sub>alkyl, cyanoC<sub>1</sub>-C<sub>6</sub>alkyl, C<sub>1</sub>-C<sub>6</sub>alkoxy, haloC<sub>1</sub>-C<sub>6</sub>alkoxy, C<sub>2</sub>-C<sub>6</sub>alkyl ether, C<sub>1</sub>-C<sub>6</sub>alkanoyl, -(SO<sub>2</sub>)R<sub>d</sub>, -N(R<sub>x</sub>)S(O)<sub>m</sub>R<sub>d</sub>, and -N[S(O<sub>m</sub>)R<sub>x</sub>]S(O)<sub>m</sub>R<sub>d</sub>; wherein m is 1 or 2, R<sub>x</sub> is hydrogen or C<sub>1</sub>-C<sub>6</sub>alkyl, and R<sub>d</sub> is C<sub>1</sub>-C<sub>6</sub>alkyl, haloC<sub>1</sub>-C<sub>6</sub>alkyl, amino, mono- or di-(C<sub>1</sub>-C<sub>6</sub>alkyl)amino or a 5- to 10-membered, N-linked heterocyclic group, each of which R<sub>d</sub> is substituted with from 0 to 2 substituents independently chosen from halogen, hydroxy, cyano, amino, nitro, mono- and di-(C<sub>1</sub>-C<sub>6</sub>alkyl)amino, C<sub>1</sub>-C<sub>4</sub>alkyl, haloC<sub>1</sub>-C<sub>4</sub>alkyl, C<sub>1</sub>-C<sub>4</sub>alkoxy and haloC<sub>1</sub>-C<sub>4</sub>alkoxy.

15. (Currently amended) A compound or pharmaceutically acceptable form salt or hydrate thereof according to claim 13, wherein:

Ar<sub>1</sub> is pyridyl, unsubstituted or substituted with halogen, cyano, C<sub>1</sub>-C<sub>4</sub>alkyl or haloC<sub>1</sub>-C<sub>4</sub>alkyl; and

Ar<sub>2</sub> is phenyl or pyridyl, substituted with from 0 to 2 substituents independently chosen from halogen, C<sub>1</sub>-C<sub>4</sub>alkyl, cyanoC<sub>1</sub>-C<sub>4</sub>alkyl, haloC<sub>1</sub>-C<sub>4</sub>alkyl, C<sub>2</sub>-C<sub>6</sub>alkyl ether and groups of the formula -(SO<sub>2</sub>)R<sub>d</sub>, wherein R<sub>d</sub> is C<sub>1</sub>-C<sub>4</sub>alkyl or haloC<sub>1</sub>-C<sub>4</sub>alkyl.

16. (Currently amended) A compound or pharmaceutically acceptable form salt or hydrate thereof according to claim 13, wherein:

Ar<sub>1</sub> is phenyl, unsubstituted or substituted with halogen, cyano, C<sub>1</sub>-C<sub>4</sub>alkyl or haloC<sub>1</sub>-C<sub>4</sub>alkyl; and

Ar<sub>2</sub> is phenyl or pyridyl, substituted with from 0 to 2 substituents independently chosen from halogen, C<sub>1</sub>-C<sub>4</sub>alkyl, cyanoC<sub>1</sub>-C<sub>4</sub>alkyl, haloC<sub>1</sub>-C<sub>4</sub>alkyl, C<sub>2</sub>-C<sub>6</sub>alkyl ether and groups of the formula -(SO<sub>2</sub>)R<sub>d</sub>, wherein R<sub>d</sub> is C<sub>1</sub>-C<sub>4</sub>alkyl or haloC<sub>1</sub>-C<sub>4</sub>alkyl.

17. (Currently amended) A compound or pharmaceutically acceptable form salt or hydrate thereof according to claim 13, wherein:

$\text{Ar}_1$  is pyridin-2-yl, 3-methyl-pyridin-2-yl, 3-trifluoromethyl-pyridin-2-yl or 3-halo-pyridin-2-yl; and

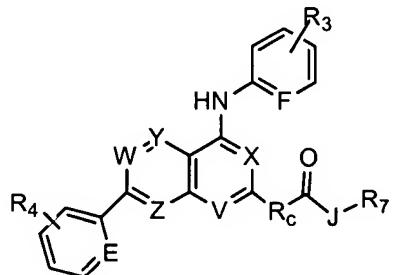
$\text{Ar}_2$  is phenyl, pyridin-2-yl or pyridin-3-yl, each of which is substituted at the *para*-position with halogen, cyano, methyl, ethyl, propyl, isopropyl, *t*-butyl, trifluoromethyl, 2,2,2-trifluoroethyl, 2,2,2-trifluoro-1-methyl-ethyl, methanesulfonyl, ethanesulfonyl, propanesulfonyl, propane-2-sulfonyl, trifluoromethanesulfonyl or 2,2,2-trifluoroethanesulfonyl.

18. (Currently amended) A compound or pharmaceutically acceptable form salt or hydrate thereof according to claim 13, wherein:

$\text{Ar}_1$  is phenyl, 2-methyl-phenyl, 2-trifluoromethyl-phenyl or 2-halo-phenyl; and

$\text{Ar}_2$  is phenyl, pyridin-2-yl or pyridin-3-yl, each of which is substituted at the *para*-position with halogen, cyano, methyl, ethyl, propyl, isopropyl, *t*-butyl, trifluoromethyl, 2,2,2-trifluoroethyl, 2,2,2-trifluoro-1-methyl-ethyl, methanesulfonyl, ethanesulfonyl, propanesulfonyl, propane-2-sulfonyl, trifluoromethanesulfonyl or 2,2,2-trifluoroethanesulfonyl.

19. (Currently amended) A compound or pharmaceutically acceptable form salt or hydrate thereof according to claim 2, wherein the compound has the formula:



wherein:

$R_c$  is C<sub>0</sub>-C<sub>2</sub>alkyl;

J is O or N( $R_z$ );

$R_z$  is:

- (a) hydrogen;
- (b)  $C_1$ - $C_6$ alkyl,  $C_2$ - $C_6$ alkenyl,  $C_2$ - $C_6$ alkynyl,  $C_3$ - $C_6$ alkanone $C_2$ - $C_6$ alkanone,  $C_2$ - $C_6$ alkyl ether, or a 4- to 10-membered carbocycle or heterocycle, each of which is substituted with from 0 to 6 substituents independently chosen from halogen, hydroxy, cyano, amino, nitro, -COOH, aminocarbonyl,  $C_1$ - $C_6$ alkyl,  $C_1$ - $C_6$ alkoxy,  $C_2$ - $C_8$ alkoxycarbonyl,  $C_2$ - $C_8$ alkanoyloxy,  $C_1$ - $C_8$ alkylthio,  $C_2$ - $C_8$ alkyl ether, and mono- and di-( $C_1$ - $C_6$ alkyl)amino; or
- (c) joined to  $R_7$  to form a 5- to 7-membered carbocycle or heterocycle that is substituted with from 0 to 6 substituents independently selected from halogen, hydroxy, cyano, amino, nitro, -COOH, aminocarbonyl,  $C_1$ - $C_6$ alkyl,  $C_1$ - $C_6$ alkoxy,  $C_2$ - $C_8$ alkoxycarbonyl,  $C_2$ - $C_8$ alkanoyloxy,  $C_1$ - $C_8$ alkylthio,  $C_2$ - $C_8$ alkyl ether, and mono- and di-( $C_1$ - $C_6$ alkyl)amino;

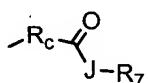
E and F are independently CH or N;

$R_3$  represents from 0 to 2 substituents independently chosen from halogen, cyano, -COOH,  $C_1$ - $C_6$ alkyl, halo $C_1$ - $C_6$ alkyl, hydroxy $C_1$ - $C_6$ alkyl,  $C_2$ - $C_6$ alkyl ether,  $C_1$ - $C_6$ alkanoyl, aminosulfonyl, mono- and di-( $C_1$ - $C_8$ alkyl)aminosulfonyl, ( $C_1$ - $C_8$ alkyl)sulfonyl, amino, and mono- and di-( $C_1$ - $C_6$ alkyl)amino;

$R_4$  represents from 0 to 2 substituents independently chosen from halogen, cyano,  $C_1$ - $C_6$ alkyl, halo $C_1$ - $C_6$ alkyl, amino, mono- and di-( $C_1$ - $C_6$ alkyl)amino, aminosulfonyl, and mono- and di-( $C_1$ - $C_8$ alkyl)aminosulfonyl; and

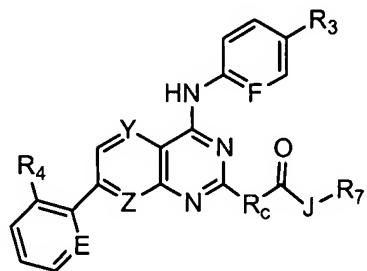
$R_7$  is:

- (i) hydrogen;
- (ii)  $C_1$ - $C_6$ alkyl, phenyl or 5- to 7-membered heterocycle, each of which is substituted with from 0 to 3 substituents independently chosen from halogen, hydroxy, cyano, amino, nitro, -COOH, aminocarbonyl,  $C_1$ - $C_6$ alkyl,  $C_1$ - $C_6$ alkoxy,  $C_1$ - $C_8$ alkoxycarbonyl,  $C_2$ - $C_8$ alkanoyloxy,  $C_1$ - $C_8$ alkylthio,  $C_2$ - $C_8$ alkyl ether $C_4$ - $C_8$ alkyl ether, mono- and di-( $C_1$ - $C_6$ alkyl)amino; or
- (iii) joined to  $R_z$  to form an optionally substituted 5- to 7-membered heterocycle; and wherein the group designated:



comprises at least one carboxylic acid group.

20. (Currently amended) A compound or pharmaceutically acceptable form salt or hydrate thereof according to claim 19, wherein the compound has the formula:



wherein:

Y and Z are independently CH or N;

R<sub>3</sub> is halogen, cyano, -COOH, C<sub>1</sub>-C<sub>6</sub>alkyl, haloC<sub>1</sub>-C<sub>6</sub>alkyl, amino, or mono- or di-(C<sub>1</sub>-C<sub>6</sub>alkyl)amino;

R<sub>4</sub> is halogen, cyano, C<sub>1</sub>-C<sub>6</sub>alkyl, haloC<sub>1</sub>-C<sub>6</sub>alkyl, amino, or mono- or di-(C<sub>1</sub>-C<sub>6</sub>alkyl)amino; and

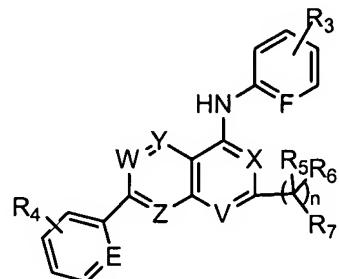
R<sub>7</sub> is (i) hydrogen; (ii) C<sub>1</sub>-C<sub>6</sub>alkyl substituted with from 0 to 3 substituents independently chosen from halogen, hydroxy, amino, -COOH, C<sub>1</sub>-C<sub>6</sub>alkoxy, and mono- and di-(C<sub>1</sub>-C<sub>6</sub>alkyl)amino; or (iii) joined to R<sub>2</sub> to form an optionally substituted 5- to 7-membered heterocycle.

21. (Currently amended) A compound or pharmaceutically acceptable form salt or hydrate thereof according to claim 20, wherein J is O.

22. (Currently amended) A compound or pharmaceutically acceptable form salt or hydrate thereof according to claim 21, wherein R<sub>7</sub> is hydrogen.

23. (Currently amended) A compound or pharmaceutically acceptable form salt or hydrate thereof according to claim 20, wherein J is NH.

24. (Currently amended) A compound or pharmaceutically acceptable form, salt or hydrate thereof according to claim 2, wherein the compound has the formula:



wherein:

E and F are independently CH or N;

R<sub>3</sub> represents from 0 to 2 substituents independently chosen from halogen, cyano, -COOH, C<sub>1</sub>-C<sub>6</sub>alkyl, haloC<sub>1</sub>-C<sub>6</sub>alkyl, hydroxyC<sub>1</sub>-C<sub>6</sub>alkyl, C<sub>2</sub>-C<sub>6</sub>alkyl ether, C<sub>1</sub>-C<sub>6</sub>alkanoyl, aminosulfonyl, mono- and di-(C<sub>1</sub>-C<sub>8</sub>alkyl)aminosulfonyl, (C<sub>1</sub>-C<sub>8</sub>alkyl)sulfonyl, amino, and mono- and di-(C<sub>1</sub>-C<sub>6</sub>alkyl)amino;

R<sub>4</sub> represents from 0 to 2 substituents independently chosen from halogen, cyano, C<sub>1</sub>-C<sub>6</sub>alkyl, haloC<sub>1</sub>-C<sub>6</sub>alkyl, amino, mono- and di-(C<sub>1</sub>-C<sub>6</sub>alkyl)amino, aminosulfonyl, and mono- and di-(C<sub>1</sub>-C<sub>8</sub>alkyl)aminosulfonyl;

each R<sub>5</sub> and R<sub>6</sub> is independently selected from hydrogen, hydroxy and C<sub>1</sub>-C<sub>8</sub>alkyl substituted with from 0 to 2 substituents independently selected from R<sub>d</sub>;

R<sub>7</sub> is:

- (i) -COOH; or
- (ii) C<sub>2</sub>-C<sub>8</sub>alkoxycarbonyl, C<sub>2</sub>-C<sub>8</sub>alkanoyloxy, C<sub>1</sub>-C<sub>8</sub>alkoxy, mono- or di-(C<sub>1</sub>-C<sub>8</sub>alkyl)amino, or a 5- to 7-membered heterocycle, each of which is substituted with from 0 to 3 substituents independently chosen from R<sub>d</sub>; or
- (iii) -PO<sub>3</sub>(R<sub>w</sub>)<sub>2</sub> or -OPO<sub>3</sub>(R<sub>w</sub>)<sub>2</sub>, wherein each R<sub>w</sub> is independently chosen from:
  - (a) hydrogen; and
  - (b) C<sub>1</sub>-C<sub>8</sub>alkyl, phenylC<sub>0</sub>-C<sub>8</sub>alkyl and (5- to 7-membered heterocycle)C<sub>0</sub>-C<sub>8</sub>alkyl each of which is substituted with from 0 to 3 substituents independently chosen from R<sub>d</sub>;

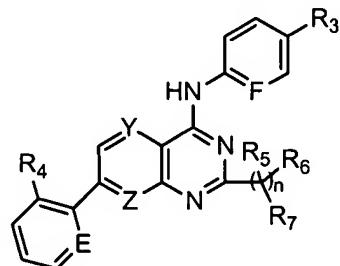
n is 0, 1, 2 or 3; and

each R<sub>d</sub> is independently chosen from:

(i) halogen, hydroxy, cyano, amino, nitro, -COOH; and  
 (ii) C<sub>1</sub>-C<sub>4</sub>alkyl, C<sub>2</sub>-C<sub>4</sub>alkenyl, C<sub>4</sub>-C<sub>4</sub>alkenyl, C<sub>1</sub>-C<sub>4</sub>alkynyl, C<sub>1</sub>-C<sub>4</sub>alkoxy, C<sub>1</sub>-C<sub>4</sub>alkanoyl, C<sub>2</sub>-C<sub>4</sub>alkoxycarbonyl, C<sub>2</sub>-C<sub>8</sub>alkanoyloxy, C<sub>1</sub>-C<sub>4</sub>alkylthio, C<sub>2</sub>-C<sub>4</sub>alkyl ether, and mono- and di-(C<sub>1</sub>-C<sub>4</sub>alkyl)amino, each of which is substituted with from 0 to 3 substituents independently chosen from hydroxy, halogen, amino and -COOH; and

wherein R<sub>7</sub> is a carboxylic acid, phosphate or phosphonate group or at least one of R<sub>5</sub>, R<sub>6</sub> or R<sub>7</sub> comprises at least one substituent selected from a carboxylic acid, phosphate or phosphonate group.

25. (Currently amended) A compound or pharmaceutically acceptable form salt or hydrate thereof according to claim 24, wherein the compound has the formula:



wherein:

Y and Z are independently CH or N;

R<sub>3</sub> is halogen, cyano, -COOH, C<sub>1</sub>-C<sub>6</sub>alkyl, haloC<sub>1</sub>-C<sub>6</sub>alkyl, amino, or mono- or di-(C<sub>1</sub>-C<sub>6</sub>alkyl)amino;

R<sub>4</sub> is halogen, cyano, C<sub>1</sub>-C<sub>6</sub>alkyl, haloC<sub>1</sub>-C<sub>6</sub>alkyl, amino, or mono- or di-(C<sub>1</sub>-C<sub>6</sub>alkyl)amino;

each R<sub>5</sub> and R<sub>6</sub> is independently hydrogen or methyl; and

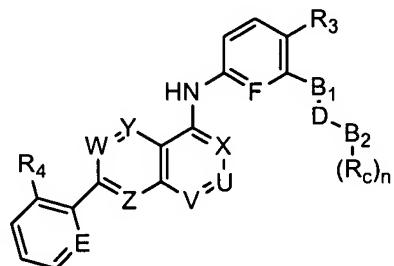
R<sub>7</sub> is:

- (i) -COOH;
- (ii) C<sub>1</sub>-C<sub>8</sub>alkoxy, C<sub>1</sub>-C<sub>8</sub>alkoxycarbonyl, pyrrolidine, piperidine, piperazine or morpholine, each of which is substituted with from 1 to 3 substituents

independently chosen from  $R_d$ , wherein at least one occurrence of  $R_d$  is a carboxylic acid group; or

(iii)  $-PO_3(R_w)_2$  or  $-OPO_3(R_w)_2$ .

26. (Currently amended) A compound or pharmaceutically acceptable form salt or hydrate thereof according to claim 2, wherein the compound has the formula:



wherein:

E and F are independently CH or N;

$R_3$  represents from 0 to 2 substituents independently chosen from halogen, cyano, -COOH,  $C_1-C_6$ alkyl, halo $C_1-C_6$ alkyl, hydroxy $C_1-C_6$ alkyl,  $C_2-C_6$ alkyl ether,  $C_1-C_6$ alkanoyl, aminosulfonyl, mono- and di-( $C_1-C_8$ alkyl)aminosulfonyl, ( $C_1-C_8$ alkyl)sulfonyl, amino, and mono- and di-( $C_1-C_6$ alkyl)amino;

$R_4$  represents from 0 to 2 substituents independently chosen from halogen, cyano,  $C_1-C_6$ alkyl, halo $C_1-C_6$ alkyl, amino, mono- and di-( $C_1-C_6$ alkyl)amino, aminosulfonyl, and mono- and di-( $C_1-C_8$ alkyl)aminosulfonyl;

$B_1$  is O, NH or S;

D is  $-C(=O)-$  or  $C_2-C_3$ alkyl, unsubstituted or substituted with a keto group; and

$B_2$  is:

- (a) O or S; in which case n is 1, and  $R_c$  is hydrogen,  $PO_3H_2$ ,  $PO_3H(alkyl)$ ,  $PO_3(alkyl)_2$ ,  $C_1-C_6$ alkyl, or  $C_2-C_6$ alkyl ether, each of which alkyl moiety is substituted with from 0 to 3 substituents independently selected from  $R_d$ ; or
- (b) N, in which case n is 2, and

- (i)  $R_c$  is independently chosen at each occurrence from hydrogen and  $C_1$ - $C_6$ alkyl,  $C_2$ - $C_6$ alkenyl| $C_4$ - $C_6$ alkenyl,  $C_2$ - $C_6$ alkynyl| $C_4$ - $C_6$ alkynyl, each of which is substituted with from 0 to 3 substituents selected from  $R_d$ ; or
- (ii) both  $R_c$  moieties are joined to form, with  $B_2$ , a 5- to 8-membered heterocycloalkyl that is substituted with from 0 to 3 substituents selected from  $R_d$ ; and
- each  $R_d$  is independently:
- (i) halogen, hydroxy, cyano, amino, nitro, -COOH; and
- (ii)  $C_1$ - $C_4$ alkyl,  $C_2$ - $C_4$ alkenyl| $C_4$ - $C_6$ alkenyl,  $C_2$ - $C_4$ alkynyl| $C_4$ - $C_6$ alkynyl,  $C_1$ - $C_4$ alkoxy,  $C_1$ - $C_4$ alkanoyl,  $C_2$ - $C_4$ alkoxycarbonyl,  $C_2$ - $C_8$ alkanoyloxy,  $C_1$ - $C_4$ alkylthio,  $C_2$ - $C_4$ alkyl ether, or mono- or di-( $C_1$ - $C_4$ alkyl)amino, each of which is substituted with from 0 to 3 substituents independently chosen from hydroxy, halogen, amino and -COOH; and
- wherein the group designated:  
 $\begin{array}{c} \sim B_1 \sim D \sim B_2 \sim (R_c)_n \end{array}$
- comprises at least one carboxylic acid, phosphate or phosphonate group.

27. (Currently amended) A compound or pharmaceutically acceptable salt or hydrate according to claim 26, wherein;

- $B_1$  is O; and
- either:
- (i) D is  $-CH_2-CH_2-$  and  $-B_2-(R_c)_n$  is:
- (a) -COOH, -O-PO<sub>3</sub>H<sub>2</sub>, or -PO<sub>3</sub>H<sub>2</sub>; or
- (b) pyrrolidine, piperidine, piperazine or morpholine, each of which is substituted with -COOH; or
- (ii) D is  $-CH_2-C(=O)-$  and  $-B_2-(R_c)_n$  is:
- (a) -OH; or
- (b) pyrrolidine, piperidine, piperazine or morpholine, each of which is substituted with -COOH.

28. - 29. (Cancelled)

30. (Currently amended) A compound or pharmaceutically acceptable formsalt or hydrate thereof according to claim 1 wherein the compound has an IC<sub>50</sub> value of 10 nanomolar or less in a capsaicin receptor calcium mobilization assay.

31. (Currently amended) A pharmaceutical composition, comprising a therapeutically effective amount of at least one compound or pharmaceutically acceptable formsalt or hydrate thereof according to claim 1 in combination with a physiologically acceptable carrier or excipient.

32. (Cancelled)

33. (Currently amended) A method for reducing calcium conductance of a cellular capsaicin receptor, comprising contacting a cell expressing a capsaicin receptor with at least one compound or pharmaceutically acceptable formsalt or hydrate thereof according to claim 1, and thereby reducing calcium conductance of the capsaicin receptor.

34. - 40. (Cancelled)

41. (Currently amended) A method for inhibiting binding of vanilloid ligand to a capsaicin receptor *in vitro*, the method comprising contacting capsaicin receptor with at least one compound or pharmaceutically acceptable formsalt or hydrate thereof according to claim 1, under conditions and in an amount sufficient to detectably inhibit vanilloid ligand binding to capsaicin receptor.

42. (Currently amended) A method for inhibiting binding of vanilloid ligand to capsaicin receptor in a patient, comprising contacting cells expressing capsaicin receptor with at least one compound or pharmaceutically acceptable formsalt or hydrate thereof according to claim 1, in an amount sufficient to detectably inhibit vanilloid ligand binding to cells expressing a cloned capsaicin receptor *in vitro*, and thereby inhibiting binding of vanilloid ligand to the capsaicin receptor in the patient.

43. - 44. (Cancelled)

45. (Currently amended) A method for treating a condition responsive to capsaicin receptor modulation in a patient, comprising administering to the patient a capsaicin receptor modulatory amount of at least one compound or pharmaceutically acceptable ~~form~~salt or hydrate thereof according to claim 1, and thereby alleviating the condition in the patient.

46. - 48. (Cancelled)

49. (Currently amended) A method for treating pain in a patient, comprising administering to a patient suffering from pain a capsaicin receptor modulatory amount of at least one compound or pharmaceutically acceptable ~~form~~salt or hydrate thereof according to claim 1, and thereby alleviating pain in the patient.

50. - 55. (Cancelled)

56. (Currently amended) A method for treating itch in a patient, comprising administering to a patient a capsaicin receptor modulatory amount of a compound or pharmaceutically acceptable ~~form~~salt or hydrate thereof according to claim 1, and thereby alleviating itch in the patient.

57. (Currently amended) A method for treating cough or hiccup in a patient, comprising administering to a patient a capsaicin receptor modulatory amount of a compound or pharmaceutically acceptable ~~form~~salt or hydrate thereof according to claim 1, and thereby alleviating cough or hiccup in the patient.

58. (Currently amended) A method for treating urinary incontinence in a patient, comprising administering to a patient a capsaicin receptor modulatory amount of a compound or pharmaceutically acceptable ~~form~~salt or hydrate thereof according to claim 1, and thereby alleviating urinary incontinence in the patient.

59. - 73. (Cancelled)